REMARKS

The Official Action dated August 26, 2003 has been carefully considered. Accordingly, the changes presented herewith, taken with the following remarks, are believed sufficient to place the present application in condition for allowance. Reconsideration is respectfully requested.

By the present Amendment, claims 1 and 8 have been amended to correct typographical errors and to more clearly define the chromatographic separation which is provided by the claimed methods and apparatus, in accordance with the teachings throughout the present specification, including the Examples and Fig. 2A. Additionally, claims 11-23 are added. Support for claims 11 and 12 may be found in claim 1 while support for claim 13 may be found in claim 8. Support for claims 14-23 can be found in the specification at page 7, lines 21-23 and page 12, lines 7-8. It is believed that these changes do not involve any introduction of new matter, whereby entry is believed to be in order and is respectfully requested.

Claims 1-7 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Examiner questioned how the ion-exchange functional groups participate in the assay method.

This rejection is traversed and reconsideration is respectfully requested. More particularly, claim 1 recites a chromatographic assay method which comprises, inter alia, providing a polymeric membrane type flow matrix which is attached to a liquid-impervious backing and permits a capillary force assisted lateral flow therethrough. At least part of the flow matrix contains ion-exchange functional groups selected from a specified group. The method further comprises initiating a first lateral flow of aqueous fluid to transport a sample

through the flow matrix and chromatographically separate each of two components from one another and from the sample as they flow along the lateral flow matrix.

As set forth in the present specification, for example at page 4, beginning at line 18 and continuing through page 5, line 17, and in the example described at pages 9-12, the ion-exchange groups facilitate the chromatographic separation based on the difference in isoelectric points of the components, i.e., based on the difference in charge between the components.

There is no requirement in 35 U.S.C. §112, second paragraph, for an applicant to recite the function of claimed components, or to recite in claims the scientific basis of an invention. In fact, an inventor need not even comprehend the scientific principles on which the practical effectiveness of an invention rests, *Fromson v. Advance Offset Plate, Inc.*, 219 U.S.P.Q. 1137, 1140 (Fed. Cir. 1983). Thus, the present claims need not recite how the ion-exchange functional groups participate in the assay method in order to comply with the requirements of 35 U.S.C. §112, second paragraph. Moreover, the Examiner has not indicated any term in claims 1-7 which is indefinite to one of ordinary skill in the art. It is therefore submitted that the rejection has been overcome. Reconsideration is respectfully requested.

Claims 1-10 were rejected under 35 U.S.C. §103(a) as being unpatentable over the Pristoupil publication entitled "Microchromatography and Microelectrophoresis on Nitrocellulose Membranes," *Chromatography Review*, 12:109-125 (1970). The Examiner asserted that Pristoupil teaches the use of nitrocellulose membrane in chromatography and electrophoresis separation of proteins and nucleic acid. The Examiner further asserted that Pristoupil teaches that the membrane is laid flat on a glass plate in a chromatography chamber and although Pristoupil does not specifically recite a membrane comprising the ion-exchange

functional groups of claim 1, Pristoupil teaches a membrane having ion-exchange function and it would be routine experimentation for one of ordinary skill in the art to employ the claimed groups. In response to Applicants' previous arguments, the Examiner asserted that the functional action of the ion-exchange groups have not been properly recited and although Applicants appear to argue that the ion-exchange groups bind the proteins and aid in their separation, such is not recited in the claims.

However, as set forth in detail below, Applicants submit that the chromatographic assay methods defined by claims 1-7 and the chromatographic devices defined by claims 8-10 are nonobvious over and patentably distinguishable from Pristoupil. Accordingly, this rejection is traversed and reconsideration is respectfully requested.

More particularly, claim 1 is directed to a chromatographic assay method which comprises providing a polymeric membrane type flow matrix attached to a liquid impervious backing, which flow matrix permits a capillary force assisted lateral flow therethrough and is a porous polymer material with pores in the range of 0.01-20 μm, treating the flow matrix to reduce or eliminate non-specific adsorption properties of the flow matrix, applying to the flow matrix a sample containing at least two components, initiating a first lateral flow of aqueous fluid to transport the sample through the flow matrix and chromatographically separate each of the two components from one another from the sample as they flow along the lateral flow matrix, interrupting the lateral flow, and detecting at least one of the separated components according to specified procedures. According to claim 8, the chromatographic device comprises a polymeric membrane type flow matrix attached to a liquid-impervious backing, which membrane permits a capillary force assisted lateral flow therethrough and contains ion exchange functional groups. The flow matrix is a porous polymer material with pores in the range of 0.01-20 μm and is adapted to chromatographically separate each of at

least two components from one another and from a sample containing the components as they flow along the lateral flow matrix.

Claims 1 and 8 both recite that the ion-exchange functional groups are selected from the group consisting of diethyl aminoethyl (DEAE), trimethyl hydroxypropyl (QA), quaternary aminoethyl (QAE), quaternary aminomethyl (Q), diethyl-(2-hydroxypropyl)-aminoethyl, triethyl aminomethyl (TEAE), triethylaminopropyl (TEAP), polyethyleneimine (PEI), methacrylate, carboxymethyl (CM), orthophosphate (P), sulfonate (S), sulfoethyl (SE) and sulfopropyl (SP) groups.

As set forth in the present specification, for example at page 2, beginning at line 17, it has surprisingly been found that the chromatographic separation employing a flow matrix as defined in claims 1 and 8 and containing ion-exchange functional groups provides a simple, fast and inexpensive analytical method for separation of biomolecules in complex mixtures. The chromatographic separation is facilitated by the ion-exchange functional groups based on differences in isoelectric points of the complex biomolecules. As described in the example set forth at pages 9-12, the methods and devices are therefore particularly suitable for separation of proteins, peptides, nucleic acids or polynucleotides having different ioselectric points.

Pristoupil discloses various analytical devices and methods. In Fig. 1 referenced by the Examiner, a chromatography device is disclosed wherein a thin hard filter paper or a perforated acetyl cellulose membrane filter fitted to a steel pin (page 113, first paragraph) is suspended using a movable support at one end. Contrary to the Examiner's assertion, Fig. 1 does not disclose a flow membrane laying flat on a glass plate. Rather, the glass plate referred to in Fig. 1 covers the entire membrane chromatography chamber.

With respect to the teachings of Pristoupil relating to ion-exchange, Applicants merely find the disclosure at page 115, paragraph 7, which states that while nitrocellulose membranes generally have a negative electrokinetic charge, the negative charge is markedly suppressed by impregnation with Tween and that titration of the ion-exchange capacity of the nitrocellulose membranes was rather low and corresponded approximately to the capacity of ordinary filter paper. One skilled in the art will clearly recognize that Pristoupil is directed to hydrophobic interaction chromatography (HIC) and adsorption chromatography, rather than ion-exchange chromatography.

Importantly, the chromatography method taught by Pristoupil adsorbs high molecular weight proteins of all types upon sample application as set forth in Fig. 3d at page 114. Pristoupil further discloses that low molecular weight components separate as a group to the front of a developing solution, as also shown in Fig. 3d at page 114.

In contrast, the chromatographic assay method of claim 1 requires chromatographic separation of each of two components from one another and from the sample as they flow along the lateral flow matrix. As discussed above, the separation is achieved as the ion exchange functional groups allow separation of the individual components based on the differences in their isoelectric points. Thus, rather than separating high molecular weight proteins as a group by initial adsorpotion and low molecular weight components as a group at the front of a developing solution, the present methods provide separation of individual components. One skilled in the art will recognize therefore that the present methods provide a significant advantage over the non-specific techniques generally disclosed by Pristoupil.

Similarly, the chromatographic device defined by claim 8 requires a polymeric membrane containing ion-exchange functional groups and adapted to chromatographically separate each of at least components from one another and from the sample containing the

components as they flow along the lateral flow matrix. As the device disclosed by Pristoupil only adsorbs high molecular weight proteins as a group and separates low molecular substances at the front of the developing solution, again as a group, Pristoupil does not teach or suggest a chromatographic device as presently claimed.

Thus, not only does Pristoupil not teach or suggest a flow matrix containing ion-exchange functional groups as recited in claims 1 and 8, Pristoupil provides no teaching or suggestion regarding the separation of individual components by use of ion-exchange functional groups in a flow matrix. To the contrary, Pristoupil, at best, discloses adsorption of high molecular weight proteins as a group and separation of low molecular weight components as a group at the front of a developing solution.

The Examiner asserts that Pristoupil could be modified through routine experimentation to result in the claimed invention. However, there is no evidence of record to support the Examiner's assertion and the specific separation of components as presently claimed, undisclosed by Pristoupil, rebuts the Examiner's assertion. Moroever, the mere fact that prior art could be modified to result in a claimed invention would not have made the modification obvious unless the prior art suggested the desirability of the modification, *In re Mills*, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Pristoupil provides no suggestion for modifying the technique disclosed therein in order to arrive at either the presently claimed chromatographic assay method or the presently claimed chromatographic device, regardless of the specific ion-exchange groups employed therein. Thus, Pristoupil does not render the presently claimed methods and devices obvious under 35 U.S.C. §103. It is therefore submitted that the methods and devices defined by claims 1-10 are nonobvious over and patentably distinguishable from Pristoupil, whereby the rejection under 35 U.S.C. §103 has been overcome. Reconsideration is respectfully requested.

It is believed that the above represents a complete response to the rejections set forth in the Official Action, and places the present application in condition for allowance.

Reconsideration and an early allowance are requested.

Respectfully submitted,

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